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SCIENCE

Creature Comforts at the Zoo

SENATOR JOHN V. TUNNEY ON GENETIC MANAGEMENT



Genetic Engineering

BY JOHN V. TUNNEY
AND MELDON E. LEVINE

Do genes enjoy civil liberties? Who owns test-tube babies?

The cry has been raised by many that the impact of science has been too fruitful. It has been raised by some with regard to the nuclear sciences. It might well be reiterated in the near future with regard to the biomedical sciences.

The biomedical sciences have provided man with the increasing ability to modify and to alter human genes. These developments touch upon the most fundamental issues of human life. They portend the ability to reshape man.

Accepted attitudes about the inviolable nature of man's genetic endowment now stand challenged by science. The political impact of this challenge might be just as powerful as the scientific impact. Unless the potential provided by the biomedical sciences is properly understood, the inevitable

social response might be fashioned out of fear. When complex problems appear too terrifying or mysterious, some people might seek simple solutions that prove inadequate or improper.

If people become sufficiently frightened—if they feel the need to be rescued from a menace they do not understand—they are more likely to delegate freedoms and less likely to respond with reason. If the polity responds to the scientific community through fear and mistrust, we could witness the erosion of our most precious freedoms. Political alteration—like genetic alteration—might be irreversible. If our personal liberty is ever lost, it might never be recovered.

Consequently, the most important and enduring of our freedoms are linked with the manner in which the biomedical sciences are understood and applied. The issues raised by the biomedical sciences must be exposed to public scrutiny. They must be discussed candidly, openly, and at once.

In approaching these issues, we

the authors must of necessity wear several "hats." The first "hat," if you will, is a multifaceted one, fashioned around our own personal backgrounds—our social, philosophical, and ethical beliefs. The second "hat" is a legal one, obtained after studying the law and participating in it over a period of years. The third is a legislative one, obtained from the unique perspective to which we are exposed in helping to propose, evaluate, and create the laws of this land.

It is important to recognize that all political figures wear "hats" of this nature. They are all different, depending upon the individual background and experience of the person, but they influence him as he evaluates and determines policy, especially in an area as sensitive and as potentially explosive as genetic engineering.

Before we discuss the ethical, legal, or legislative view, however, it is important to set forth the most salient aspects of genetic engineering and to indicate our assessment of the state of the art in each of these aspects.

John V. Tunney is the junior senator from California. Mr. Levine, a lawyer, is his legislative assistant. This article is based on an address given by the senator at the California Institute of Technology.

ABORTION AND AMNIOCENTESIS. The technique of amniocentesis—prenatal sampling of the amniotic fluid surrounding the fetus—is frequently used to provide advice on therapeutic abortions. The procedure is relatively safe, but we do not yet have the ability, with amniocentesis, to detect all genetic defects. Within five years most monogenic defects that we understand will be detectable thereby, but even then questions will remain unanswered as to whether amniocentesis affects the eventual intelligence of the child.

MASS GENETIC SCREENING. In this, too, we appear to be on the threshold. The technique is available for many diseases, although not for some others. However, it has already become evident that many people will oppose mass genetic screening—whether of children or adults—for a variety of personal reasons. Some feel it is an invasion of personal rights; others do not want children genetically defective to find out that they are so afflicted. Again, however, the technology is increasingly available.

MONOGENIC GENE THERAPY. Modification of certain cells in terms of their genes, or monogenic gene therapy, we have been advised, has not yet been performed successfully. It should, however, be a possibility for certain diseases within five years. As we gain more knowledge about monogenic defects, the possibility of monogenic gene therapy will become more of a reality in broader areas.

IN VITRO FERTILIZATION. Both in vitro fertilization and reimplantation in the uterus have been performed successfully in experimental animals. If the research in this area is not seriously inhibited by external controls, the technology for in vitro fertilization and for reimplantation in human beings should be available within five to ten years, or perhaps even earlier. Recently a Yugoslav scientist advised a conference in Tokyo that had developed an instrument for oocyte (egg) transplant into the uterus.

CLONING. Cloning of frogs, where a replica of an individual is developed from one of its somatic cells, has already been successful. The technology for the cloning of mammals will be available within five years, and, unless research is stopped, the technology for the cloning of human beings might be available within anything from ten to twenty-five years.

POLYGENIC GENE THERAPY. We are very far away from achieving polygenic gene therapy—perhaps 50 to 100 years. Our understanding of polygenic gene defects still is extremely primitive. For a variety of reasons it is considerably more complicated to isolate and trace a polygenic trait than to isolate and trace a monogenic trait.

One of the most powerful arguments presented in favor of employing one or more of the technologies of genetic engineering in the direction of genetic intervention is that man's genetic load is increasing. In other words, the total number of genetic defects carried by man has been increasing. This has been occurring as a result of the increased mutation rate that accompanies population growth and the decreased natural selection rate occasioned by modern medicine and technology. About one child in twenty, for example, is now said to be born with a discernible genetic defect.

The question then arises: Should the human species attempt to employ these new technologies to deal with this increased genetic load? Paul Ramsey of Yale has stated that "it is no answer to say that changes are already taking place in humankind or that men are constantly modifying themselves by changes now consciously or unconsciously introduced. . . ." He argues, as a Protestant theologian, that scientific intervention in this area is a questionable human aspiration, as he puts it, "to Godhood." Regardless of the merits of Ramsey's position, the very vigor with which he defends it suggests the extent to which ethical issues are at stake.

The ethical questions raised by the possibilities implicit in genetic engineering are no less fundamental than the issues of free choice, the quality of life, the community of man, and the future of man himself. Thus, it becomes evident that one's own sense of ethics, one's personal view of right and wrong, one's own standard of conduct or moral code, are essential components of decision making in this extremely sensitive area.

Many political scientists like to believe that political decision making can be objectified, that a process can be delineated by which political decisions are made. Through such a process, it is assumed, decisions and actions can be predicted. The wisdom of these political scientists is questionable for a variety of reasons. One of the most important is the significant subjective component of political decision making—the large realm left to one's own values and ethics.

This realm affects all aspects of lawmaking. It is especially important in any political or even legal approach to genetic engineering. One's own values or ethics must inevitably be brought to bear upon a variety of important questions in this area, questions that can be evaluated only by subjective criteria. In an effort to rationalize some of the issues involved, we will attempt to draw some distinctions and to articulate some criteria for analysis. Some of these criteria have been sug-

Any scientific or technical initiatives of one generation that would eliminate the options of future generations should be avoided.

gested by others; some are our own. We suggest them not as a definitive list but as a reminder that it will be very important to apply criteria such as these to any legislative or legal analysis of the implications of genetic engineering.

Let us posit a list of ten general considerations suggesting possible ethical distinctions:

First, if we are to engage in any eugenics, negative or positive, we must confront three vital questions that pervade this entire subject: What traits are to be considered desirable? Who is to make that determination? When in the course of human development will the choice be made? These questions cannot be underestimated in their importance to the future of man, particularly when we are considering biological alternatives that might not be reversible.

Second, we must ask whether the genetic engineering or "improvement" of man would affect the degree of diversity among men. Does it presume a concept of "optimum" man? Is diversity important as a goal in itself? Does—or should—man seek an "optimum," or does he seek a "unique"? What would the quest for an "optimum" do for our sense of tolerance of the imperfect? Is "tolerance" a value to be cherished?

Third, we should consider whether it might be appropriate to delineate different biological times or moments—at least in humans—during which experimentation might occur. Do different ethical considerations apply if we attempt to distinguish between experimentation on an unfertilized sperm or egg, a fertilized sperm or egg, a fetus, an infant, a child, or an adult? Might the factors to be balanced in making a decision as to whether experimentation is proper vary at different stages of human development?

Fourth, is there a workable difference between, on the one hand, genetic "therapy" to correct genetic factors known to cause somatic disease and, on the other hand, genetic "engineering," defined as techniques to alter man in terms of some parameters other than somatic disease? Might it be appropriate to attempt such a distinction in definitions in this emotionally charged area? Might the term "genetic therapy" evoke less emotionally charged reactions than the term

"genetic engineering"? Might it, in fact, be preferable to respond more receptively to those areas of genetic work that are primarily "therapeutic"? Or is such a distinction unworkable?

Fifth, it would seem to be advisable to ask whether a particular technique or technology is devised for the therapeutic treatment of an individual or whether it is designed to have a broader societal impact. This potential distinction has a variety of ramifications. For example, it should be asked whether techniques developed for the therapy of an individual patient automatically diffuse into the general public for purposes other than this therapy. Are physicians operationally capable of restricting the use to one group, or does societal pressure make them semiautomatic dispensers of seemingly desirable technologies?

Sixth, we might ask whether any eugenics program—whether positive or negative, voluntary or compulsory—does not imply a certain attitude toward "normalcy," toward a proper norm for human activity and behavior, and toward expectations with regard to the behavior of future generations of human beings. Implicit in this question are distinctions with regard to positive versus negative eugenics programs and also with regard to compulsory versus voluntary eugenics programs.

Seventh, how are words such as "normal," "abnormal," "health," "disease," and "improvement" defined? Are they words that can be operationally used to determine what should be done in the area of genetic engineering?

Eighth, we must ask if the quest for genetic improvement would be continuous. Would it invariably make all children "superior" to their parents? What would be the social consequences of this? Would it institutionalize generation gaps and isolate communities by generations?

Ninth, we should consider whether the institutionalization of a quest for genetic improvement of man is likely to lead to his perception of himself as lacking any worth in the state in which he is. What does this do to the concept of the dignity of the human being in his or her own right, regardless of some "index of performance"?

Tenth, if we have a well-developed ability to perform genetic therapy as an assault upon certain diseases but such therapy is not available for all who have the affliction or who desire the "cure," the question will immediately arise as to how to determine which patients will receive it. Are some classes or groups of people more desirable patients or more worthy of treatment? How will selection be made? By what criteria will those decisions be reached?

Questions such as these ten can be answered only by appealing to ethical, or so-called moral, arguments. When we enter this realm, it is important to remember that no one has a greater claim to wisdom than anyone else. All men have a stake in this area, and all men have a right to be heard.

We would like to offer three additional thoughts that might affect all of the ethical judgments involved. Two are caveats, and one might be a preliminary guide for analysis.

The two caveats are reminders of the imprecision of measurement and the difficulty of meaningful analysis in this area. As for the imprecision of measurement (caveat number one), Ramsey states that "many or most of the proposals we are examining are exercises in 'what to do when you don't know the names of the variables.'" While that might be somewhat harsh, he is accurate in his suggestion that prediction of behavior or even of most genetic disease will be very difficult, owing not only to polygenic factors but also to such other imponderables as pinpointing a recessive trait in its heterozygous state and predicting the influence of environmental factors.

The second caveat is the difficulty of meaningful analysis. Some values we will be asked to compare will be like comparing apples and oranges. How can one, for example, compare the possible deep satisfaction experienced by an infertile woman carrying and bearing a child that was fertilized in vitro and reimplanted in her uterus with the 1 or 2 or 5 per cent chance that the child will be deformed? In measuring eugenic traits to be cherished, how can one compare intelligence (even assuming it can be defined) with love?

In making genetic choices—and in selecting those who will make them—one should not forget such caveats.

The last of these attempts at ethical classification is an effort to ask the question of just where in the broad field of genetic engineering the ethical issues will arise. At what level in the process? Professor Abram Chayes of Harvard Law School has suggested that at least three levels can be discerned at which the questions posed above might arise:

First, the general level of research. Should research be pursued that might lead to technologies that will give science the genetic capability to engineer human beings?

Second, the level of treating human disease. Questions will, of course, be raised as to what exactly is a disease—and how it is defined. (Should socially undesirable or disruptive behavior be treated as an illness? Are some forms of mental illness proper candidates for genetic therapy?) Even assuming that those questions can be answered, eth-

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ical considerations will arise with regard to whether the disease should be treated with a newly available genetic technique.

Third, the broad level of attempting to affect society—the level of what some will consider an improvement of the human species.

These levels overlap to some degree with the questions we have already raised, and it appears clear that the ethical pressures that will be directed against the continuation of the activity will become increasingly strong as we move from the first to the second and then to the third level. While these considerations by no means exhaust the ethical realm, they do suggest the enormity of the problems with which we are attempting to deal. Perhaps the attempt—however primitive—at ethical classification might also offer the lawyer some general guidance.

It might be asked, for example, whether there are legal as well as ethical distinctions between negative and positive eugenics. Are there legal differences between an attempt, on the one hand, to treat an individual for disease by either monogenic or polygenic gene therapy and an attempt, on the other hand, to control behavior or otherwise alter society's norms? Does it matter—legally—at what point in the state of human development the therapy or the engineering is conducted: whether in the stage of birth control, in the realm of abortion, in treating a minor or an adult? Does it matter—legally—how the therapy or the engineering is conducted, whether it is voluntary or compulsory, whether for punitive or eugenic reasons, or whether the physician has freely and openly obtained the consent of the patient?

Clearly, these distinctions ought to be important—legally as well as ethically. They touch upon fundamental and traditional legal principles, principles that have been applied in Anglo-American jurisprudence for a number of years. They offer the lawyer a variety of factors that will help in his analysis.

Law, at least in the United States, can be said to operate on three broad tiers or levels. First, we have constitutional law, or the legal framework set forth by the Constitution of the United States and by the courts in interpreting the Constitution. Second, we have

statutory law, or law that is enacted by statute—either of a state or of the federal government. No statute can contravene a constitutional requirement. But, in the absence of a constitutional prohibition or pre-emption, federal and state legislatures can enact statutory standards to respond to a variety of needs, such as those that arise in the areas of health and welfare. Third, in the absence of a controlling constitutional or statutory provision, the courts rely upon the body of law known as the common law—those legal principles that have emerged from judicial decisions. The issues raised by the technology of genetic engineering affect constitutional, statutory, and common-law principles. We shall briefly consider each of these legal tiers.

At least three constitutional factors clearly emerge when one considers the general subject of genetic engineering. The first is the right to privacy. The Fourth Amendment to the Constitution declares that "the right of the people to be secure in their persons, houses, papers, and effects, against unreasonable searches and seizures, shall not be violated. . . ." This language has been interpreted to guarantee to the individual a constitutional right of privacy. Genetic engineering raises questions with regard to the extent and inviolability of that right. The second factor involves the rights protected in the Fifth and Fourteenth amendments, which guarantee that no person shall be deprived of life, liberty, or property without due process of law. Third, and perhaps the most important factor that the Constitution brings to bear upon genetic engineering, is the *approach* of constitutional law—the method of analysis that courts have developed for dealing with constitutional issues. Apart from the technicalities inherent in whether state action is or is not involved—a threshold question in any constitutional analysis—constitutional law requires the government to show a more compelling governmental need when the abridgment of fundamental freedoms is involved.

Let us take two examples. Contrast, for instance, a government-sponsored compulsory program of negative eugenics, designed to eliminate a certain genetic disease, with a government-sponsored compulsory program of positive eugenics, designed to control behavior. As both programs are compulsory, both could infringe the fundamental freedom of procreation and possibly of marriage. However, compelling state interest could be advanced as a more legitimate argument in eliminating a disease rather than in controlling or altering behavior. The eradication of disease has long been accepted as a vital social objective.

We do not offer this dichotomy in an effort to support the negative eugenics program. In fact, we would probably oppose it. But we do think that a constitutional analysis of the two approaches would bring different factors into being and might yield different results in the two cases.

To move from constitutional law to statutory law, it should be noted at the outset that a variety of statutes in numerous American jurisdictions have attempted to impose eugenics controls. Professor William Vukowich of Georgetown has written: "In the early 1900s, many states enacted laws that prohibited marriage by criminals, alcoholics, imbeciles, feeble-minded persons, and the insane. Today most states prohibit marriage by persons with venereal disease but only a few states have laws which are similar to those of the early 1900s. Washington and North Dakota, however, still prohibit marriage by women under forty-five and men of any age, unless they marry women over forty-five, if they are an imbecile, insane, a habitual criminal, a common drunkard, feeble-minded or [a] person who has . . . been afflicted with hereditary insanity."

A number of the more recent developments in the field of genetic engineering, however, go entirely unregulated. Sperm banks—which may be used as a reserve of sperm for artificial insemination by third-party donors, for example—are an excellent example of institutions for which pertinent statutes do not exist. Their administration is entirely up to the persons operating them.

That is an instance in which our third legal tier, the tier of the common law, must be our guide. In the absence of constitutional or statutory guidance, we must turn to the common law for our standards. Here again the law is neither silent nor comprehensive. It falls somewhere in between. Assume this set of possibilities: Amniocentesis is an everyday practice, held by most doctors to be free of harmful effects such as infection. A woman who has not been offered amniocentesis gives birth to a Mongoloid child. Is her obstetrician liable for malpractice?

Common-law tort principles of malpractice would probably hold that the doctor would, in fact, be liable. This is so because the common law in determining negligence tends to follow whatever is the accepted medical practice for a particular community. But is this a viable solution? Would it be appropriate to require amniocentesis even if the mother—or the doctor—has strong religious convictions that preclude consideration of an abortion under any circumstances? What about offering amniocentesis under those circumstances? And what about the legal

rights of an egg that has been fertilized and grown in a test tube? Does the *father* have any rights? What rights does the *mother* have? Or the doctor? Do common-law tort or property rights apply to this question?

However one evaluates these issues, they must be faced. If one does not wish to face them with the exclusive guidance of the common law, the result will be the consideration of new legislation. To the extent that current law is inadequate, legislation must be developed.

In considering the possibility that legislation must be developed, we both are painfully aware of the potential inadequacy of the legal and the legislative processes in responding to issues presented by science. In the area of genetic engineering, science may be outpacing the legal and legislative processes. It may be presenting challenges to which our lawyers and legislators are ill-equipped to respond. Our legislative system may be poorly equipped to respond to these problems because of at least two inherent difficulties: its speed and its scope.

Our legislative process generally works slowly. Sen. Walter Mondale, for example, first introduced legislation that called for a commission to study the effects of genetic engineering almost five years ago. That bill passed the Senate unanimously last year, but it has not yet been acted upon by the House of Representatives. Just initiating a study commission on so momentous a subject has already, then, taken longer than five years.

Not only is our political system slow. It is, obviously, only national in scope. Generally, that is not a significant problem to the people in Washington who are considering various legislative proposals. Most proposals are only national in scope—or less. Genetic engineering, however, is clearly a matter of international concern. It will require, if any controls or guidelines are to be effectively suggested, international agreements. This also will serve as a political or legislative constraint.

Recognizing these constraints, we still believe that certain constructive steps can be taken—steps that will begin to offer legislative rationalization to the field. If the legislative system begins to consider these problems now, it might be possible to respond politically and legislatively before it is too late.

Conversely, we fear the consequences that could be wrought if informed legislative consideration of the issues inherent in genetic engineering does not soon begin. If the legislation comes as a result of dramatic scientific breakthroughs that scare the public, the outcome might be hasty and unwise political decisions predicated

upon inadequate information and upon fear. If debates and discussions begin now, however, the ultimate legislation might emanate from deliberate and reasoned political, social, and scientific analysis. We do not believe that, at this point, it would be appropriate to suggest answers to the momentous issues raised by genetic engineering. But we do believe that we know enough to undertake certain legislative initiatives. Let us suggest three.

First, Congress should enact the Mondale bill [S. J. Res. 75], which provides for a study and evaluation of the ethical, social, and legal implications of advances in biomedical research and technology. The proposed study commission might serve as a preliminary vehicle for educating the public about the foreseeable social consequences of biological advances. Such a commission might best be an international one, but that is logically a second step.

Second, and perhaps equally important, is the initiation of technology assessment in all institutions that disburse funds, direct research, or provide grants that are related to biomedical concerns. It has long been obvious that technological developments have implications that affect society in a variety of ways and that their impact cannot be limited to an analysis of the technical aspects of the product or of the innovation. Similarly, the myriad implications of the developments of biomedical research reach out to all segments of society. Technological assessment should be a part of any analysis of any project that involves a potentially new biomedical development.

Third, it might be appropriate for Congress to earmark a small proportion of health research funds (say one-quarter or one-half of 1 per cent) for research into possible social consequences of biological technologies either presently available or foreseeable.

It is not only the legislature, however, that can initiate improvement in communication between the scientific community and the general public as well as expansion of public awareness of and concern with these issues. Four other suggestions might be worthy of consideration:

First, private foundations should be urged to initiate programs to bridge presently existing gaps between the sciences and the humanities, exposing people in each area to people in the other, and making the ideas of each readily available and understandable to the other.

Second, universities should consider establishing additional programs whereby students in the humanities would be exposed to the methodologies familiar to those in the scientific disciplines, and vice versa. The two gen-

eral groups should feel a closer relation to and understanding of each other in universities as well as elsewhere. The effective separation of these two groups in universities—particularly at the graduate level, but even at the undergraduate level—establishes a line of demarcation between those in the sciences and those in the humanities, with very inadequate and narrow bridges to unite the two general areas.

Third, research proposals in the biological area should perhaps be assessed by institutional research review committees that include nonscientists. Some form of technological assessment, in other words, or consideration of the ethical, moral, and social implications of biological projects—by nonscientists—should be considered at the level of all research proposals in this general area.

Fourth, it might be appropriate for the medical profession itself to study the ways in which the technologies it uses for the benefit of individual patients may affect society as a whole if used for purposes other than the cure of individual patients. The "individual treatment versus social engineering" dichotomy should be considered clearly and carefully by the medical profession and should probably be emphasized more strongly than it currently is.

These efforts to bring society and the biomedical sciences closer together are, in our opinion, essential. Dr. Andre Hellegers, director of the Joseph and Rose Kennedy Institute for the Study of Human Reproduction and Bioethics of Georgetown University, has testified before the Senate that "nothing could be worse than that society should come to fear scientific progress. . . . I can foresee that the occasional, seemingly sensational, scientific episode will so frighten society as to undermine the very support [that] science needs in order to continue to make contributions to improve the lot of mankind. . . . It is high time that there be started an educative process that explains to the country the precise nature and limitations of the scientific process and the place it occupies in man's control of his environment. . . . No segment can stand apart in this interdependent society. If it attempts to do so, it is bound to cease being supported. The sooner the relationship of science to society is examined and explained for all to see, the better it will be both for science and for society."

This testimony touches upon two very important facts of American political life, neither of which should be forgotten. First is the theory of political accountability; if the public supports something financially, the public is entitled to know what it is that it is supporting. Second is the foundation of political democracy; thoughts, sug-

What about the legal rights of an egg that has been fertilized and grown in a test tube? Does the *father* have any rights? The *mother*?

gestions, proposals, and policies should be scrutinized in the market place of ideas. Political debate and public discussion are healthy and are conducive to the best analysis of any position. Particularly in an area as fraught with subjectivity as this one, it is vital that the issues raised be aired, discussed, and debated. We are dealing in an area in which there is no monopoly of expertise. Rather, it is a field in which men trained in a variety of different areas, or even in no special area, bring to bear their own unique perspective, or, if you will, "expertise." We are dealing with a subject in which morality, or one's own subjective sense of ethics, is pervasive. We are, therefore, dealing with an area in which all persons have a right and a special claim to be heard.

There are certain suggestions that we would offer in any debate on this subject. We would suggest that among the values that man ought to protect most fully are the values of humility, of compassion, of diversity, and of skepticism. We would suggest that any scientific or technical initiatives of one generation that would foreclose or eliminate the options of future generations—any decision today that implies an ability to predict the human traits that will be most cherished tomorrow—smacks of arrogance and should be avoided. We would suggest that man should exercise the utmost caution in this sensitive field and that decisions that will be genetically irreversible might require a wisdom we do not possess. We would also suggest that there is no reason why the ethics or morality of any one of us is better than that of any other. In the realm of morality each of us has an equal claim to wisdom.

Therefore, the issues raised by the biomedical scientists must be debated, and the debate must begin now. If we postpone debate in this area, we might face irreversible trends not only in genetics but also in political freedoms.

All segments of society should be involved in the debate these new technologies demand. The techniques must be discussed and debated among lawyers, doctors, theologians, legislators, scientists, journalists, and all other segments of society. The issues raised require interdisciplinary attention. We cannot begin too soon to consider them. □